



## Swiss Science Concentrates

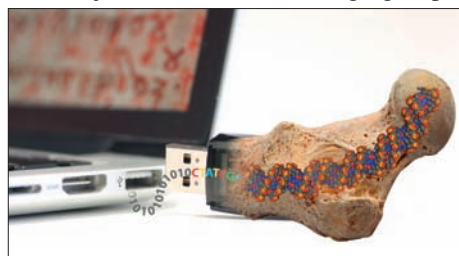
A CHIMIA Column

Short Abstracts of Interesting Recent Publications of Swiss Origin

### Robust Chemical Preservation of Digital Information on DNA in Silica with Error-Correcting Codes

R. N. Grass\*, R. Heckel, M. Puddu, D. Paunescu, and W. J. Stark, *Angew. Chem. Int. Ed.* **2015**, 54, 2552. ETH Zürich

The conservation of digital information for extended time frames is challenging and cannot be guaranteed by traditional optical and magnetic storage technologies. DNA has been proposed as a potential medium for long-term data storage but several limitations, especially in terms of desiccated DNA preservation and error handling, exist. Grass, Stark and coworkers now showed that digital information can be recovered from DNA after encapsulation in an inorganic matrix and by employing error-correcting codes. Thus, the *Swiss Federal Charter from 1291* and the *Method of Archimedes* (83 kB of information) were translated into 4991 158-mers of DNA. The DNA was encapsulated in silica and subjected to accelerated aging experiments. The original

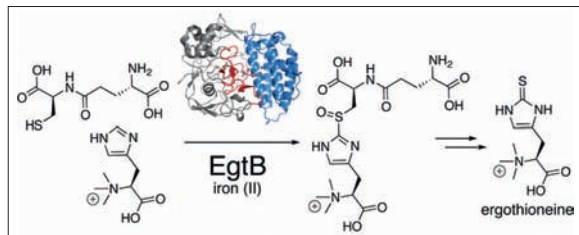


information could be recovered error free after keeping the DNA at 70 °C for one week, conditions that are equivalent to storage in central Europe for 2000 years.

### Structure of the Sulfoxide Synthase EgtB from the Ergothioneine Biosynthetic Pathway

K. V. Goncharenko, A. Vit, W. Blankenfeldt\*, and F. P. Seebeck\*, *Angew. Chem. Int. Ed.* **2015**, 54, 2821. University of Basel

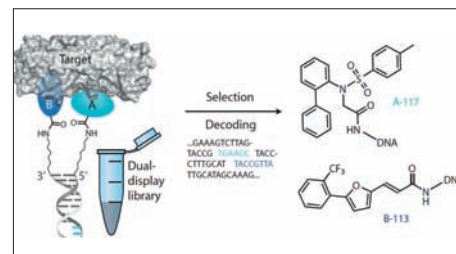
Ergothioneine occurs in a broad range of prokaryotic and eukaryotic organisms, including humans and human pathogens such as *Mycobacterium tuberculosis*. The precise cellular function of ergothioneine is not known, but recent observations suggest that this sulfur compound may be a protectant against oxidative stress. To elucidate the structural basis for sulfoxide synthase activity, Seebeck, Blankenfeldt and coworkers have endeavoured and successfully achieved the crystal structure of EgtB from *Mycobacterium thermoresistibile* in complex with  $\gamma$ -glutamyl cysteine and N- $\alpha$ -trimethyl histidine. The study reveals that the two substrates and three histidine residues serve as ligands in an octahedral iron binding site. This active site geometry is consistent with a catalytic mechanism in which C–S bond formation is initiated by an iron(III)-complexed thyl radical attacking the imidazole ring of N- $\alpha$ -trimethyl histidine.



### Dual-display of Small Molecules Enables the Discovery of Ligand Pairs and Facilitates Affinity Maturation

M. Wichert, N. Krall, W. Decurtins, R. M. Franzini, F. Pretto, P. Schneider, D. Neri\*, and J. Scheuermann\*, *Nat. Chem.* **2015**, 7, 241. ETH Zürich

Dual-display DNA-encoded chemical libraries allow the identification of fragment pairs that bind simultaneously to a biological target molecule. However,

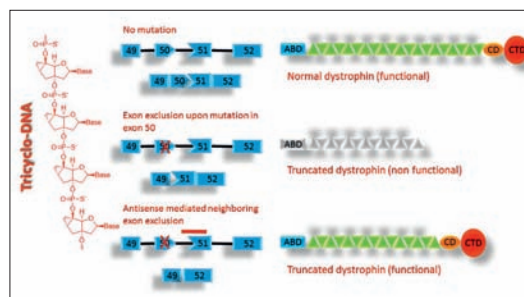


the technology has been limited by difficulties in the decoding process. Scheuermann, Neri and coworkers now report a strategy that overcomes this limitation. Small organic molecules were conjugated to complementary DNA strands that contain a unique identifying code. DNA hybridization followed by an inter-strand code-transfer created a DNA-encoded chemical library of 111,100 members (see illustration; with permission, NPG). Using this approach, a low micromolar binder to  $\alpha$ -1-acid glycoprotein and a ligand to carbonic anhydrase IX has been identified, which dramatically improved tumour targeting performance *in vivo*.

### Functional Correction in Mouse Models of Muscular Dystrophy Using Exon-skipping Tricyclo-DNA Oligomers

A. Goyenvallé, G. Griffith, A. Babbs, S. El Andaloussi, K. Ezzat, A. Avril, B. Dugovic, R. Chaussonot, A. Ferry, T. Voit, H. Amthor, C. Bühr, S. Schürch, M. J. A. Wood, K. E. Davies, C. Vailland, C. Leumann\*, and L. Garcia\*, *Nat. Med.* **2015**, 21, 270. University of Bern

Systemic use of antisense oligonucleotides (AONs) is limited due to poor tissue uptake. Garcia, Leumann and collaborators present a new class of AONs made of tricyclo-DNA (tcDNA), which displays unique pharmacological properties and unprecedented uptake by many tissues after systemic administration. Improved properties were demonstrated in mouse models of Duchenne muscular dystrophy (DMD), a neurogenetic disease in the dystrophin gene. The findings render tcDNA-AON chemistry particularly attractive as a potential future therapy for patients with DMD and other neuromuscular disorders or with other diseases that



are eligible for exon skipping approaches requiring whole-body treatment.